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January 22, 1992

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January 22, 1992
Date of Signature

UTSK:097

FILE:

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

RE: SN 07/313,911 - **"METHOD AND APPARATUS FOR DIRECT MEASUREMENT OF HEMOGLOBIN SPECIES IN WHOLE BLOOD"** -- Shepherd, et al. (UTHSC/SA:097)

Dear Sir:

Enclosed for filing is:

(1) Reply to Examiner's Answer, **in triplicate;**

(2) Supplemental Information Disclosure Statement, PTO-1449 and reference (1);

(3) Petition for a Two Month Extension of Time up to and including January 22, 1992; and

(4) Check in the amount of $175.00 for the basic filing fee for a two month extension of time (small entity).

Please stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Kevin L. Daffer
Reg. No. 34,146

KLD/as.13
Enclosures

#19

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
A.P. Shepherd, et al.

Serial No.: 07/313,911

Filed: February 23, 1989

For: METHOD AND APPARATUS FOR DIRECT MEASUREMENT OF HEMOGLOBIN SPECIES IN WHOLE BLOOD

§

Group Art Unit: 255

Examiner: R. Rosenberger

Atty. Dkt.: UTSK:097/DAF

92-099

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REPLY TO EXAMINER'S ANSWER

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

This paper is submitted in reply to the Examiner's Answer mailed October 22, 1991. The period for filing this reply brief having expired November 22, 1991, filed herewith is a petition for extinction of time, with appropriate fee, extending the time period for filing this Reply Brief for two months to and including January 22, 1992.

The Examiner's Answer appears to contain new points of argument which this Reply Brief addresses as permitted under 37 C.F.R. § 1.193(b). In particular, four new points of argument appear to have been raised in the Examiner's Answer on pages 3-12 beginning with section 11 "Response to argument". This Reply Brief addresses those four new points of argument in the order in which they were levied.

In response to the first new point of argument raised on page 3, line 2 - page 6, line 2 of the Examiner's Answer, Appellants

wish to point out that while Anderson studies three wavelengths virtually identical with the wavelengths in the present application (specification: page 7), the wavelengths in Anderson produce more radiation scattering than the present invention as evidenced by a comparison of Figs. 2 and 6 of Anderson with Fig. 5 of the present invention. The difference in the level of scattering is attributed to the physical dissimilarities between the integrating sphere methodology of Anderson and the methodology of the claimed invention.

Although Anderson studies several wavelengths within the range of the present invention, Anderson does not suggest that the studied wavelengths have high extinction coefficients or produce minimal scattering. More importantly, Anderson makes no suggestion that wavelengths which do have minimal scattering, given its integrating sphere apparatus, would be <u>determined to distinguish one constituent component from another</u> (Claim 1). For example, a wavelength having minimal scattering may produce a higher optical density for one specific hemoglobin species and not for the other species as shown in Fig. 4 of the present application. Thus, a chosen linear wavelength with minimal scattering may help distinguish one component species from the other given the known optical density relationship between each constituent species. Neither Anderson nor Brown disclose this relationship or a method by which species can be distinguished from one another as in present Claim 1.

The Examiner's Answer indicates that since the resulting wavelengths selected in Anderson and Brown are virtually identical to the present wavelengths, the method by which the wavelengths are selected are not patentably different. Appellants respectfully traverse. In particular, as stated above, the method of Claim 1 does not minimize scattering by merely searching for wavelengths with high extinction coefficients as in Anderson. The claimed method calculates concentrations of at least three component

species by irradiating the sample with at least three corresponding radiation frequencies. Such a method is not disclosed in Anderson or Brown. In addition, the method of Claim 1 as recited above, distinguishes each component species based on the radiation frequency chosen for a corresponding component species demonstrating a maximum optical density for that species. Nowhere does Anderson or Brown disclose such a distinguishing methodology.

In response to the second new point of argument, presented on page 6, line 3 - page 7, line 7 of the Examiner's Answer, Appellants reassert that Anderson and Brown cannot be properly combined. While Appellants acknowledge a relationship between hemolyzed and non-hemolyzed blood, Appellants find no reason why a person given the Anderson reference could discern the equivalence of measuring methodologies using hemolyzed, diluted blood with measuring methodologies using non-hemolyzed blood. The idea of there being a mere physical relationship certainly does not suggest that one may combine one method with another method simply based upon that relationship. In particular, optical density sensors which employ hemolyzed blood have been well known in the prior art. Nevertheless, there is no suggestion that the blood in such art not be hemolyzed and that three or more component species be analyzed from the non-hemolyzed blood as in the present Claim 1.

In response to the third new point of argument, presented on page 7, line 8 - page 9, line 23 of the Examiner's Answer, Appellants reassert that Anderson does not suggest wavelengths be chosen to distinguish constituent components. Contrary to the Examiner's position, Appellants find no relationship whatsoever of "conventional spectrophotometric techniques" taught in Anderson to the present method step of choosing wavelengths to distinguish constituent components. On page 7, lines 11-20 of the Examiner's Answer, the argued relationship between Anderson's spectrophotometric techniques and the present method of distinguishing constituent components is not understood. Nowhere

in Anderson is there an implication that the spectrophotometric techniques purposefully selects an irradiating frequency used to distinguish one component from the other. Certainly, the Examiner does not mean to imply such a relationship.

Furthermore, Appellants do not understand how the Examiner can infer that it would be at least obvious for a person reading Anderson to choose a wavelength which can distinguish a constituent component merely on the basis that Anderson discusses oxyhemoglobin component and that oxyhemoglobin is one of the constituent components discussed in Brown. The logic behind the Examiner's argument lodged on page 7, line 21 - page 8, line 2 is not understood by the Appellant and appears irrelevant.

With reference to the Examiner's statement on page 8, lines 15-24, Appellants concur that Brown referenced "whole blood." However, the initial fluid material of Brown is whole blood. To perform measurement, the initial whole blood of Brown is diluted and then irradiation (Brown - col 6, lines 36-56; col 13, lines 52-68). Note that each of the claims of Brown discuss preparing the sample by aspirating, diluting and/or hemolyzing the sample mixture in order for the apparatus and method to function properly. Thus, while Brown may disclose whole blood, it does not suggest that whole blood be analyzed as in Anderson and the present invention. Since Anderson teaches analysis of whole, undiluted blood and Brown teaches analysis with diluted, hemolyzed blood, Appellants reassert that their intended functions would be destroyed if the hypothetical combination were made. Furthermore, there is a disincentive for making the combination, since one reference (Anderson) clearly teaches away from the other reference (Brown) and vice versa.

With reference to the Examiner's statement on page 9, lines 1-23 of the Examiner's Answer, Appellants reassert that Brown does not teach or suggest that the wavelengths used in its device be

chosen as having high extinction coefficients as proposed by Anderson. Brown does not make such a selection based upon the magnitude of extinction coefficients as taught in Anderson. In fact, Brown only presents the selected wavelengths but does not disclose how those wavelengths were selected (Brown - col 3, lines 29-36). While it may be true that the resulting wavelengths have high extinction coefficients, it is not necessarily true that they were chosen, like Anderson, because they have high extinction coefficients.

In response to the fourth new point of argument, presented on page 10, line 1 - page 12, col 12 of the Examiner's Answer, Appellants wish to point out that Claims 1 and 8 - 12 are separately patentable, while Claims 2 - 7 stand or fall with Claim 1. The Examiner's statements with respect to Claims 2 - 7 have no bearing unless combined with independent Claim 1. None of the cited art discloses the method steps of Claim 1 and accordingly, do not disclose the method of claim 1 in combination with the method of generating white light (Claim 6) or tunable lasers (7).

Appellants reassert that neither Anderson nor Brown make mention of light-emitting diodes (Claim 8), controlled monochromators (Claim 9), or controlled diffraction ratings (Claim 10) as potential frequency sources. By generating a plurality of radiation frequencies, the claimed invention can identify one selected radiation frequency with a corresponding constituent component (Claim 11) which is neither taught or suggested in the cited art. The radiation frequencies, being equal in number to the constituent components are not taught in Brown as suggested by the Examiner. Instead, Brown suggests that at each of four wavelengths, four molar extinction coefficients or four hemoglobin species are determined (Brown - col. 3, lines 34-36).

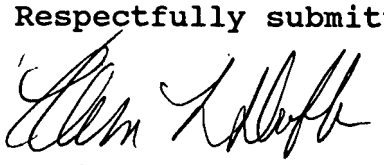
Appellants reassert that the Shibata reference in not within the field of the present claimed art, nor is it reasonably

pertinent to the unique problems with which the claimed invention is involved. Shibata teaches a spectrophotometer without suggesting the spectrophotometer be used to measure constituent components of blood. A skilled artisan would not look toward a spectrometer used to obtain absorption spectrum in order to render certain features of the spectrometer applicable to a method of measuring hemoglobin species in whole blood.

CONCLUSION

For all of the above reasons, and for reasons clearly stated in Appellants brief mailed July 26, 1991, it is believed that the claims patentably distinguish over the art of record. Appellants respectfully request that the Board of Patent Appeals overturn the Examiner's rejections.

Respectfully submitted,



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